

**PATHOLOGY AND BACTERIOLOGY**

UNDER THE CHARGE OF

OSKAR KLOTZ, M.D., C.M.,

PROFESSOR OF PATHOLOGY AND BACTERIOLOGY, UNIVERSITY OF PITTSBURGH,  
PITTSBURGH, PA.

**Movements of Tissues in Culture Media.**—LOEB and FLEISHER (*Jour. Med. Res.*, 1917, xxxvii, 75) give a resumé of their previous work and include some new experiments in this significant problem, which, being merely in its infancy, permits of but provisional conclusions. The authors consider three factors of importance in determining the movement of tissue cells which are brought in contact with culture media: (1) a factor recognizable for the initial sending out of pseudopodia, the primary desequilibrizing factor; (2) the contact with solid bodies which strongly influence the direction in which the cells move; (3) a centrifugal force driving the cells into the coagulum and away from the tissues. In other words, an innate centrifugal tendency and an outside factor, the stimulating action of contact with a solid body. This mode of reaction they have called stereotropism, which is based on surface changes occurring in cells under the influence of variations in the surrounding medium. Such modifications in the cell surface lead to a viscid condition of the ectoplasm, causing it to stick to solid bodies, thus causing the initial desequilibration as well as the movements in contact with foreign bodies, such as threads. It may be expected that the stimulus calling forth the sending out of pseudopodia affects especially that side of the cells which adjoins the coagulum (of blood plasma) while the other side adjoining the tissue is less affected. This condition itself would tend to lead to a movement in the direction of the coagulum. As to the centrifugal movement of cells away from their tissue base into the coagulum it is probable that the principal factor is the negative chemotropic influence which living cells exert upon one another together with the positive attraction for the cells, exerted by certain constituents of a clot or necrotic materials, and also the mechanical factors as of contact and the polarized change in the environment of the cells. The presence of dead tissue is the factor that directly or indirectly determines the direction of movements of various kinds of cells, but this stimulus is absent under ordinary conditions in the body. Connective-tissue cells, and to a less extent differentiated epithelial cells and carcinoma, move actively in a coagulum *in vitro*, but not in the normal organism. Epithelial cells from the guinea-pig in a culture medium of coagulated blood serum were seen to grow and to divide mitotically without any association with connective tissue, behaving essentially like ameba and moving less freely than connective-tissue cells. The growth of the latter, on account of their importance in the formation of scar tissue, is of special interest. There are many factors which influence their growth into the coagulum. For this work the authors used pieces of rabbit kidney into which incisions had been made five to eleven days previous to the experiment in order to increase

the number of fibroblasts. The degree of contact between coagulum and tissue is of importance, since the fibroblasts do not grow across a space such as may be formed by the action of fibrolyns. The ingrowth of cells is more rapid if the fibers of the coagulum are parallel to those of the tissue, and the degree of hardness and the character of the surface of the coagulum are of significance; the immigration is the more difficult the denser the coagulum and the smoother its surface. The fibroblasts travel by sending out pseudopodia along the lines of the fibrils of the coagulum. The authors noticed among the fibroblasts certain ones which seemed to have a phagocytic function. As to the movement of other tissue cells in the coagulum, that of kidney tubule cells and of mouse carcinoma cells is slight. In most of these experiments growth was at its height three days after placing the tissues into the culture media; after seven days all the cells in coagulum and media were necrotic.

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**The Incidence of Bovine Infection of Tuberculosis in Man.**—Careful analyses of the infecting microorganism in tuberculosis of man are relatively few. We have gradually had it impressed upon us that the tubercle bacillus present in various tissue lesions was not always of the same kind. The attitude of Koch, in 1901, gave the impression that we need look for only one type of bacillus, the human, in studying the nature of the infective microorganism in pulmonary lesions. Newer methods of technic have given us an opportunity of studying the tubercle bacillus with greater ease, and have also opened the way for distinguishing the various types of these organisms and demonstrating their presence in human lesions. With these newer methods at hand, WANG (*Jour. Path. and Bact.*, 1917, xxi, 131) has isolated tubercle bacilli from a variety of sources. The organisms were then studied and tested to determine the type. Of 123 strains of tubercle bacilli obtained from 88 cases of tuberculosis in man, all conformed with the regular human or bovine type. Bovine bacilli were isolated 7 times in an examination of sixty-eight adults and the same microorganism was obtained 11 times from twenty children. These bovine bacilli were found in the sputum, lymph glands, abdomen, and meninges. The high percentage (55) of bovine infection in children under sixteen is striking. The author believed that the distribution of lesions as found at autopsy indicated the intestinal route of infection in 50 per cent. of the children, while in adults it fell to 13 per cent. In studying other analyses of the incidence of bovine infection in Edinburgh the author finds that in a total of 281 cases in which the type of tubercle bacillus was determined, 78 per cent. in children under five, 70 per cent. in children from five to sixteen, and 7.8 per cent. in adults over sixteen were of bovine type. The author was also able to show that tuberculous processes which had undergone calcareous change still retained some of the original infection.

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**Spirocheta Morsus Muris the Cause of Rat-bite Fever.**—Much interest has recently been shown in studies upon rat-bite fever. In all there have been over 80 cases of human infection reported in the literature. The disease in man has definite clinical manifestations, among which the periodic recurrence of the fever, swelling of lymph glands and the appearance of a skin rash are the most important. There is

usually an incubation period of from ten to twenty-two days. Schottmüller reported the finding of a streptothrix in the enlarged lymph glands of a patient, and this was subsequently confirmed by Blake, who was able to cultivate the microorganism. Shortly following this, Tunnicliff reported upon the finding of a similar streptothrix in the lungs of rats suffering from chronic bronchopneumonia. Her findings suggested that the rat was subject to spontaneous infection by this microorganism, and that during the infectious stage was capable of transferring infections to man. Shortly following the report by Blake, a brief report from Japan claimed the finding of a spirochete in the blood and tissues of 2 patients with rat-bite fever. These same authors, FUTAKI, TAKAKI, TANIGUCHI and OSUMI (*Jour. Exper. Med.*, 1917, xxv, 33) bring further evidence of the specific nature of a spirochete for this disease. They have had the opportunity of studying 5 more cases, in each of which the spirochete has been demonstrated and in 2 the microorganism was found in the circulating blood. The authors clearly point out that the disease under discussion is one having clinical manifestations as detailed above. It is pointed out that the rat may serve as a carrier for a variety of microorganisms pathogenic to man, and that the various infections may be transmitted through bites. The spirochete which they have found is larger than the *Spirocheta pallida*, and, furthermore, possesses a flagellum. With difficulty the microorganism is demonstrated directly in the lesions of man, but is more easily shown when infected tissues are inoculated into mice. Mice, rats, guinea-pigs and monkeys may all be infected. In the monkey a disease may be induced having some of the manifestations observed in the human cases. The spirochete has been successfully cultivated. Associated with this work, ISHIWARA, OHTAWARA and TAMURA (*Jour. Exper. Med.*, 1917, xxv, 45) carried on a series of animal experiments. Eighty rats were caught and were made to bite guinea-pigs. Of this number, 10 produced experimental rat-bite fever in the exposed animals. They have been unable to detect the spirochete in the mouth of the infected rats. The clinical course of the disease in the guinea-pig resembled that in man, though the progress of the fever was not as regular. The disease could be propagated to new animals by the inoculation of blood or tissue emulsions obtained from the originally infected guinea-pigs. Upon infecting rats or mice, the spirochete could be demonstrated in the peripheral blood. These authors are not as yet convinced that the spirochete which they have demonstrated is identical with that isolated by Futaki and his co-workers. The spirochetes of Ishiwarra is short and appears to possess a flagellum at each end. The spirochetes disappear from the blood of infected animals by the use of salvarsan.

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**Fistula in Ano and Tuberculosis.**—The causal relationship between fistula and tuberculosis has been a much discussed question. STONE (*Am. Rev. Tuberculosis*, 1917, i, 548) quotes Melchior as finding 61 per cent. of his fistulæ tuberculous, whereas Frey found a similar relationship in only 6.9 per cent. of 72 cases; the latter relied entirely upon a microscopic finding of a typical lesion, but the former, in addition to this, bases his figures on a diagnosis of tuberculosis elsewhere, usually in the lungs, present before, after or at the time of the fistula. Of 123

cases seen by the author, 31 were carefully examined for tuberculosis; 13 presented active lesions and 7 showed evidence of previous involvement of the lungs. Microscopic examination of tissue from 10 fistulae, all but 2 of which were from the groups which had either active or inactive tuberculosis, showed only one containing tubercles. Nevertheless, from his own experience and from that of others, he feels that there is a causal relationship between fistula and tuberculosis in 15 per cent. to 30 per cent. of the cases, while the characteristic lesion in the fistula can be demonstrated in only about 10 per cent. A corollary to this is the author's final conclusion that in a considerable percentage of cases no relationship exists between fistula in ano and tuberculosis.

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**Contributions to the Biochemistry of Pathogenic Anaerobes.**—

Starting with the assumption that the effect of anaerobes is mainly local and the changes brought about lend themselves readily to analytical study, WOLF and HARRIS (*Jour. Path. and Bact.*, 1917, xxi, 386) have thrown much light on the biochemistry of *B. welchii* and *B. sporogenes*. These two anaerobes serve as examples of the saccharolytic and proteolytic groups of Henry. The authors made careful investigations on gas production, ammonia and amino-acid formation, production in tritratable acidity as well change in hydrogen-ion concentration and the sugar consumption of these bacteria with a variety of media. The methods employed are relatively simple. Different strains of the two anaerobes were used in practically all of the experiments which make it somewhat difficult to compare the various results. The results obtained are important. *B. welchii* in a medium containing 3 or 4 per cent. of lactose may give a volume of gas 3.8 times that of the medium used. Gas produced in sugar-free media such as casein is difficult to explain and the authors suggest that it may be due to the production of amino-acids which may be glycogenetic. In the experiments with peptone water prepared from casein the amino-acids appear to have provided the pabulum for gas production. The velocity of gas production shows a latent period, a sharp rise and then a secondary rise. The composition of the gas first formed was on one occasion 90 per cent. hydrogen while the relationship of hydrogen to carbon dioxide in the final composition was roughly 2.1. The activity of growth of *B. welchii* and its death are closely associated with the hydrogen-ion concentration, and it would appear that the optimum is at or below  $P_H=4.9$ , and the lethal point between  $P_H=4.52$  to  $P_H=4.56$ . The importance of the amino-acids is indicated by the increase in these substances before gas production took place. Volatile acids made up about 60 per cent. of the total acidity, and of this nearly all was normal butyric acid. The *B. sporogenes* shows many marked differences. The amount of gas produced is almost as much as that by *B. welchii*, and it produces it in practically all media. The amount of gas formed by *B. sporogenes* is the same in 4 per cent. alkaline casein and sugar in addition. The *B. sporogenes* takes longer to establish itself and produce gas on many of the media than does *B. welchii*, but during this period it is very active in amino-acid production. The proteolytic enzymes of this anaerobe attack media in which extensive proteolysis has already taken place. Ammonia was formed in one experiment

in quantities to more than balance the original amino-acids present in the medium (peptone water). In alkaline casein 20 per cent. of the total nitrogen originally present is transformed into ammonia. The strongly basic properties of ammonia are important. Butyric acid is formed by *B. sporogenes* as well as other organic acids. In conclusion, the author suggests the possibility of using a solution, for treatment of wounds with *B. welchii* present, in which the hydrogen-ion concentration is  $\text{pH} = 4.5$ . The article is filled with suggestions for much future work and will stimulate biochemical investigations of bacterial activity.

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## HYGIENE AND PUBLIC HEALTH

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UNDER THE CHARGE OF

MILTON J. ROSENAU, M.D.,

PROFESSOR OF PREVENTIVE MEDICINE AND HYGIENE, HARVARD MEDICAL SCHOOL,  
BOSTON, MASSACHUSETTS,

AND

GEORGE W. McCOY, M.D.,

DIRECTOR OF HYGIENIC LABORATORY, UNITED STATES PUBLIC HEALTH SERVICE,  
WASHINGTON, D. C.

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**Pneumonia.**—A great advance in our knowledge of pneumonia has recently been achieved through the work of COLE (*Arch. Int. Med.*, 1914, xiv, 56), DOCHEZ and GILLESPIE (*Jour. Am. Med. Assn.*, 1913, lxi, 727), HANES (*Jour. Exper. Med.*, 1914, xix, 38), AVERY (*Jour. Exper. Med.*, 1915, xxii, 105). Four groups or strains of pneumococci are now recognized: (1) being all diplococci they can be differentiated only by their agglutination reactions with specific sera, except Group III, which is morphologically characteristic. Group I is the cause of from 30 to 47 per cent. of all cases of pneumonia and has a mortality of about 24 per cent. Group II is indistinguishable from Group I save by the agglutination reaction. It is found in from 18 to 39 per cent. of cases and is fatal in about 60 per cent. of cases caused by it. Immune sera (2) produced by each of these two groups have been obtained from horses and seem to have specific therapeutic value. Group III is the *Pneumococcus mucosus* (3) formerly classified with the *Streptococcus mucosus*. It has a distinct mucoid capsule and produces an abundant, stringy mucous growth on surface colonies. It is the cause of from 8 to 13 per cent. of all pneumonia and is fatal in about 61 per cent. of cases. Group IV comprises a heterogenous lot of pneumococci not classified with Groups I, II or III. Each strain of cocci in this group produces a specific agglutinin for itself, which does not agglutinate the other strains or groups. This is the type ordinarily found in normal mouths. These organisms are of low virulence, cause about 20 per cent. of cases, and have a mortality of only about 7 per cent. These four groups seem quite stable and show no tendency to mutation. The pneumococci of the first three groups cause about 80 per cent. of all cases of pneu-